

Listing of Claims

1. (Previously presented) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.
2. (Previously presented) The antibody-based fusion protein of claim 1, 49, or 51, wherein said amino acid substitution increases the hydrophobicity of said antibody-based fusion protein.
3. (Canceled)
4. (Previously presented) The antibody-based fusion protein of claim 49 or 51, wherein said substitution changes the C-terminal amino acid of the Ig chain.
5. (Previously presented) The antibody-based fusion protein of claim 1, wherein said non-Ig protein is a secreted protein.
6. (Previously presented) The antibody-based fusion protein of claim 5, wherein said non-Ig protein is a mature form of said secreted protein.
7. (Previously presented) The antibody-based fusion protein of claim 49 or 51, wherein the Ig chain comprises part of an Ig heavy chain.
8. (Previously presented) The antibody-based fusion protein of claim 49 or 51, wherein the Ig chain comprises at least the CH2 domain of an IgG2 or an IgG4 constant region.
9. (Canceled)
10. (Canceled)

11. (Previously presented) The antibody-based fusion protein of claim 7, wherein said part of an Ig heavy chain further has binding affinity for an immunoglobulin protection receptor.

12. (Previously presented) The antibody-based fusion protein of claim 7, wherein said Ig chain has substantially reduced binding affinity for a Fc receptor selected from the group consisting of Fc γ RI, Fc γ RII and Fc γ RIII, when compared to the binding affinity of an unsubstituted Ig chain for said Fc receptor.

13. (Previously presented) The antibody-based fusion protein of claim 1, wherein said non-Ig protein is selected from the group consisting of a cytokine, a ligand-binding protein, and a protein toxin.

14. (Original) The antibody-based fusion protein of claim 13, wherein said cytokine is selected from the group consisting of a tumor necrosis factor, an interleukin, and a lymphokine.

15. (Original) The antibody-based fusion protein of claim 14, wherein said tumor necrosis factor is tumor necrosis factor alpha.

16. (Original) The antibody-based fusion protein of claim 14, wherein said interleukin is interleukin-2.

17. (Original) The antibody-based fusion protein of claim 14, wherein said lymphokine is a lymphotoxin or a colony stimulating factor.

18. (Previously presented) The antibody-based fusion protein of claim 17, wherein said colony stimulating factor is a granulocyte-macrophage colony stimulating factor.

19. (Original) The antibody-based fusion protein of claim 13, wherein said ligand-binding protein is selected from the group consisting of CD4, CTLA-4, TNF receptor, and an interleukin receptor.

20-23. (Canceled)

24. (Previously presented) The fusion protein of claim 1, 49 or 51, further comprising a linker between said Ig chain and said non-Ig protein.

25-28. (Canceled)

29. (Previously presented) The fusion protein of claim 1 further comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within the Ig chain, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without the amino acid substitutions.

30-35. (Canceled)

36. (Previously presented) The fusion protein of claim 4 wherein the C-terminal amino acid of said N-terminal Ig chain is substituted.

37-45. (Canceled)

46. (Previously presented) The fusion protein of claim 1, 49, 51, or 57, wherein said hydrophobic or non-polar amino acid is selected from the group consisting of Leu, Trp, Ala, and Gly.

47. (Previously presented) The fusion protein of claim 1, wherein said hydrophobic or non-polar amino acid is Ala.

48. (Canceled)

49. (Previously presented) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising an IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain and an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.

50. (Previously presented) The antibody-based fusion protein of claim 49 wherein the constant domain comprises at least one of a CH1, CH2, or CH3 domain.

51. (Previously presented) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising:

at least one of a CH2 and CH3 domain; and

an amino acid sequence that is non-natural within 10 amino acids from its C-terminus, the non-natural amino acid sequence comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid, wherein the antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.

52. (Previously presented) The antibody-based fusion protein of claim 51 wherein the Ig chain is an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE chain.

53. (Previously presented) The antibody-based fusion protein of claim 4 wherein the Ig chain comprises the CH2 domain of the IgG2 constant region and a C-terminal lysine is substituted with a nonpolar or hydrophobic amino acid.

54. (Previously presented) The antibody-based fusion protein of claim 53, wherein the C-terminal lysine is substituted with an alanine.

55. (Previously presented) The antibody-based fusion protein of claim 53, wherein the non-Ig protein is a cytokine.

56. (Previously presented) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and a CH3 domain, and the C-terminal non-Ig protein comprising an amino acid alteration within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, the alteration introducing an amino acid selected from the group consisting of Leu and Trp, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid alteration.

57. (Previously presented) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus, the substitution replacing a charged amino acid with a hydrophobic or non-polar amino acid, wherein the antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.

58. (Previously presented) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the N-terminal Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus of the Ig chain, the substitution introducing a hydrophobic or non-polar amino acid selected from the group consisting of Ala, Gly and Trp, wherein the antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.

59. (Canceled)